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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/058,825	01/30/2002	Roderick John Scott	0623.1160001/LBB/GLL	2437
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FISH & RICHARDSON P.C.			BAUM, STUART F	
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MINNEAPOLIS, MN 55440-1022			1638	

DATE MAILED: 01/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 10/058,825	<b>Applicant(s)</b> SCOTT, RODERICK JOHN	
	<b>Examiner</b> Stuart F. Baum	<b>Art Unit</b> 1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 07 November 2005.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 20,21,62-67,69,71,76-78 and 80-93 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 20,21,62-67,69,71,76-78 and 80-93 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 30 January 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner. .  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>11/7/05, 2/25/05</u> . | 6) <input type="checkbox"/> Other: _____  |

**DETAILED ACTION**

1. The amendments filed 11/7/2005 have been entered.

***RCE Acknowledgment***

2. The request filed on 11/7/2005 for a Request for Continued Examination (RCE) under 37 C.F.R. § 1.114, based on parent Application No. 10/058,825 is acceptable and a RCE has been established. An action on the RCE follows.

Claims 1-19, 22-61, 68, 70, 72-75 and 79 have been canceled.

3. Claims 20-21, 62-67, 69, 71, 76-78, 80-93 are pending and are examined in the present office action.

***Claim Objection***

4. Claim 76 is objected to for being dependent on a rejected base claim. For purposes of compact prosecution, claim 76 will be interpreted to be dependent on claim 62. Correction is requested.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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5. Claims 20-21, 62-67, 69, 71, 76-78, and 80-93 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The rejection includes dependent claims.

Claim 20 is indefinite in the recitation “a sequence whose transcription product comprises a partial or full length Arabidopsis DNA methyltransferase 1 (Met1) sequence.” Applicants have disclosed “Therefore, the designation Arabidopsis Met1 sequence will always refer to the sequence of Accession No. L10692...” (page 13 of Remarks filed 11/7/2005, 1<sup>st</sup> full paragraph). Said sequence is a DNA sequence, therefore, it is unclear how a transcription product can be a DNA sequence and not a mRNA sequence.

Claim 62 is indefinite in the recitation “a sequence whose transcription product comprises a partial or full length Zea mays sequence orthologous to the Arabidopsis methyltransferase 1 (Met1) sequence.” Applicants have disclosed “Therefore, the designation Arabidopsis Met1 sequence will always refer to the sequence of Accession No. L10692...” (page 13 of Remarks filed 11/7/2005, 1<sup>st</sup> full paragraph). Said sequence is a DNA sequence, therefore, it is unclear how a transcription product can be a DNA sequence and not a mRNA sequence.

### ***Written Description***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 20-21, 62-67, 69, 71, 76-78, 80-93 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a

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way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a method for the production of modified endosperm comprising a sequence whose transcription product comprises a partial or full-length Arabidopsis DNA methyltransferase 1 (Met1) sequence or a partial or full-length Zea mays sequence orthologous to the Arabidopsis Met1 sequence, or wherein the transcription product comprises an antisense nucleic acid, or wherein the transcription product is a sense copy of the Zea mays or Arabidopsis sequence, or wherein the transcription product is a partial sense copy of the Zea mays or Arabidopsis sequence.

Applicant discloses subcloning the MET1 cDNA, which is 4.7kb long, isolated by RT-PCR from an Arabidopsis cDNA library using the MET1F primer of SEQ ID NO:5 and MET1R primer of SEQ ID NO:6 (page 30, Example 3). Applicants disclose that the Arabidopsis Met1 sequence was cloned by Finnegan et al (1993, Nucleic Acids Res. 21:2383-2388; listed in IDS) and that Finnegan et al disclose the Met1 sequence as Accession Number L10692 (page 12 of Remarks filed 11/7/2005, 7<sup>th</sup> paragraph). Applicants further state "Therefore, the designation Arabidopsis Met1 sequence will always refer to the sequence of Accession No. L10692..." (page 13 of Remarks filed 11/7/2005, 1<sup>st</sup> full paragraph).

The Office has included the full length Arabidopsis Met1 sequence in the written description rejection, even though the Met1 sequence was known in the prior art, because the claims are drawn in part to said sequence wherein said sequence is effective for down-regulating any methylating enzyme and not just the corresponding encoded enzyme.

Applicants do not disclose any sequence whose transcription product is a partial or full length Arabidopsis Met1 or Zea mays orthologous sequence to the Arabidopsis Met1 sequence. Applicants do not identify essential and/or unique regions of the Arabidopsis Met1 sequence, nor any partial sequences thereof, nor any partial or full sequences of the Zea mays homologue of the Arabidopsis Met1 sequence, that can be used to down-regulate one or more methylating enzymes present in a plant.

The Federal Circuit has recently clarified the application of the written description requirement to inventions in the field of biotechnology. See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In summary, the court stated that a written description of an invention requires a precise definition, one that defines the structural features of the chemical genus that distinguishes it from other chemical structures. A definition by function does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. The court goes on to say, "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus." *See University of California v. Eli Lilly and Co.*, 119 F.3d 1559; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Applicants fail to describe a representative number of sequences whose transcription product is a partial or full length sequence of the Arabidopsis Met1 sequence, or partial or full sequences of the Zea mays homologue of the Arabidopsis Met1 sequence, that can be used to down-regulate one or more methylating enzymes in any plant. Applicants only disclose a DNA

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sequence having an accession number L10692 that was known in the art prior to Applicants' filing date, wherein the sequence encodes the Arabidopsis DNA methyltransferase 1 protein, as discussed above. Furthermore, Applicants fail to describe structural features common to members of the claimed genus of polynucleotides. Hence, Applicants fail to meet either prong of the two-prong test set forth by *Eli Lilly*. Furthermore, given the lack of description of the necessary and/or unique elements of said sequences that can be used to down-regulate any methylating enzyme in any plant, it remains unclear what features identify an Arabidopsis Met1 sequence that can be used to identify the Zea mays homologue or can be used to identify partial sequences of the Arabidopsis Met1 or partial sequences of the Zea mays homologue of the Arabidopsis Met1 sequence. Since the genus of said sequences has not been described by specific structural features, the specification fails to provide an adequate written description to support the breadth of the claims.

Applicant's arguments filed 11/7/2005 have been fully considered but they are not persuasive.

Applicants contend that the instant specification discloses that the Met1 gene can be used in antisense orientation to decrease the degree of methylation (page 14 of Remarks, 2<sup>nd</sup> full paragraph). Applicants contend that whole or partial sequences can be used. Applicants contend that the nucleotide sequences for Arabidopsis and Z. mays MET1 were known in the field and cites page 32 lines 6-8 and lines 27-29 from the specification (*Ibid*). Applicants contend MET1 can be down-regulated using antisense, sense, or ribozymes directed against MET1 or combinations thereof, using germ-line promoters (page 15 of Remarks, top paragraph).

The Office contends that Applicants claims are drawn to a sequence whose transcription product comprises a partial or full-length Arabidopsis or Zea mays DNA methyltransferase 1 (Met1) sequence, wherein the introduced nucleic acid is effective for down-regulating one or more DNA methylating enzymes present in the plant. The Office interprets “a partial” sequence to comprise any two consecutive amino acids from Arabidopsis or Zea mays DNA methyltransferase 1 (Met1) protein. The Office contends that Applicant has only disclosed a nucleic acid sequence that encodes a full-length Arabidopsis Met1 protein that is effective in down-regulating the corresponding endogenous gene when transformed in Arabidopsis or in Brassica campestris and Brassica oleraceae (see below for details). Applicant has also not disclosed a full length Met1 sequence that can down-regulate any methylating enzyme. Applicant has not disclosed any partial sequence as the Office interprets “a partial” sequence, nor has Applicant disclosed any Zea mays homologous Met1 sequence. Therefore, given the disclosure of only one sequence in the recitation “Therefore, the designation Arabidopsis Met1 sequence will always refer to the sequence of Accession No. L10692...” (page 13 of Remarks filed 11/7/2005, 1<sup>st</sup> full paragraph), the Office contends that Applicant is not in possession of the broadly claimed invention.

### ***Scope of Enablement***

7. Claims 20-21, 62-67, 69, 71, 76-78, 80-93 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for increasing the amount of endosperm in an Arabidopsis or Brassica seed or increasing the weight of an Arabidopsis or Brassica seed comprising a construct comprising a full length MET1 DNA



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sequence operably linked to the AGL5 promoter, wherein the sequence is in antisense orientation, or wherein the MET1 DNA sequence is isolated by RT-PCR from Arabidopsis using the primers MET1F of SEQ ID NO:5 and MET1R of SEQ ID NO:6 and Arabidopsis and Brassica plant transformation therewith, does not reasonably provide enablement for claims broadly drawn to a method of modifying the endosperm from any plant comprising down-regulating any DNA methylating enzyme using a sequence whose transcription product comprises a partial or full length Arabidopsis Met1 sequence or which comprises a partial or full-length Zea mays sequence orthologous to the Arabidopsis Met1 sequence, or wherein the nucleic acid is a partial or full length sequence in sense or antisense orientation. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claimed invention is not supported by an enabling disclosure taking into account the *Wands* factors. *In re Wands*, 858/F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

The claims are drawn to a method for the production of modified endosperm in part comprising a transcription product comprising a partial or full-length Arabidopsis DNA

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methytransferase 1 (Met1) sequence or a partial or full-length Zea mays sequence orthologous to the Arabidopsis Met1 sequence, or wherein the transcription product comprises an antisense nucleic acid, or wherein the transcription product is a sense copy of the Zea mays or Arabidopsis sequence, or wherein the transcription product is a partial sense copy of the Zea mays or Arabidopsis sequence.

Applicant discloses subcloning a sequence that encodes the Arabidopsis MET1 protein, wherein the nucleic acid sequence is 4.7kb long, in which the sequence was isolated by RT-PCR from an Arabidopsis cDNA library using the MET1F primer of SEQ ID NO:5 and MET1R primer of SEQ ID NO:6, subcloned into a vector comprising the AGL5 or AP3 promoter in antisense orientation (page 30, Example 3; and Figures 6 and 7) and transformation into Arabidopsis (page 31, Example 4) or into Brassica campestris and Brassica oleraceae (page 33, Example 5). Plants expressing the pAGL5Met1as produced seed with increased weight (page 31, lines 26-28). Applicants disclose the mean seed weight of plants transformed with pAP3Met1as is less than that of 2x-2x seed (page 32, lines 21-22). Applicants disclose the mean seed weight of 2x-2x seed is 22 micrograms (page 31, lines 26-28). Applicants disclose “pAGL5Met1ms and pAP3Met1as were transformed into Brassica campestris and Brassica oleraceae via standard methods. Reciprocal crosses between the transgenic individuals of the two species yield plump seeds which germinate to give hybrid plants. Crosses between wild type individuals of the two species result in shrivelled seeds which fail to germinate. Hence the two transgenes overcome the normal barrier to interspecific hybridization (page 33, lines 16-21).

Re: claims 20 and 62 recite “the nucleic acid molecule comprising a promoter ... and a sequence whose transcription product...” As written, the Office broadly interprets the claim to

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mean a construct comprising a promoter and another sequence, wherein the sequence is located in a position not necessarily next to the promoter. Therefore, the promoter would not affect the transcription of the sequence. Given this interpretation of the claim, the method is not enabled because it is unclear how the sequence can be transcribed at the appropriate time and in the appropriate cells.

Applicants claims 20 and 62 recite that the nucleic acids are effective for down-regulating one or more DNA methylating enzymes which cause a decrease in DNA methylation. The state-of-the-art teaches down-regulating methylating genes produces unpredictable results. Jacobsen et al (2000, Current Biology 10:179-186) teach transforming *Arabidopsis* with a nucleic acid encoding the MET1 protein operably linked to a promoter in antisense orientation caused a decrease in methylation by 80%-90%. Jacobsen et al disclose that “Surprisingly, this work showed that the floral development gene *SUPERMAN* was ectopically hypermethylated and silenced” (page 180, left column, 1<sup>st</sup> full paragraph).

The Office interprets the recitation “comprises a partial ...sequence” to read on a great number of sequences because a partial sequence reads on any two nucleotides from applicants’ Met1 sequence. Applicant has only disclosed primer sequences to be used for isolating an *Arabidopsis* MET1 sequence from an *Arabidopsis* cDNA library. Applicants have not disclosed how one makes or isolates any of the other sequences that are encompassed by Applicants’ broad claims. Applicants have not taught which regions of the respective polynucleotides can be used to amplify, for example, the *Zea mays* orthologous sequence, or which regions can be used as a probe to isolate any of said polynucleotide sequences.

Using degenerate primers to amplify a target sequence does not always produce expected results. The state-of-the-art teaches DNA fragments do not always hybridize with the expected complementary DNA. Fourgoux-Nicol et al (1999, Plant Molecular Biology 40 :857-872) teach the isolation of a 674bp fragment using a 497bp probe incorporating stringent hybridization conditions comprising three consecutive 30 minute rinses in 2X, 1X and 0.1X SSC with 0.1% SDS at 65<sup>0</sup>C (page 859, left column, 2<sup>nd</sup> paragraph). Fourgoux-Nicol et al also teach that the probe and isolated DNA fragment exhibited a number of sequence differences comprising a 99bp insertion and a single nucleotide gap, while the DNA fragment contained 2 single nucleotide gaps and together the fragments contained 27 nucleotide mismatches. Taking into account the insertions, gaps and mismatches, the longest stretch of contiguous nucleotides to which the probe could hybridize consisted of 93bp of DNA (page 862, Figure 2).

Applicants claims are drawn to a method comprising the Arabidopsis Met1 sequence or the Zea mays homologue of the Arabidopsis Met 1 sequence, both of which are used to down regulate any methylating enzyme from any plant. In other words, using heterologous sequences to down regulate endogenous genes. Using DNA sequences to reduce expression of the endogenous corresponding gene through the mechanism of sense suppression produces unpredictable results. Gutterson (1995, HortScience 30(5):964-966) teaches that the chrysanthemum and petunia chalcone synthase (CHS) genes are 70% identical to each other, and that transforming petunia plants with the chrysanthemum CHS gene did not co-suppress the endogenous petunia CHS gene (page 965, left column, second paragraph). Gutterson reports similar data using another petunia gene in the anthocyanin pathway.

The state-of-the-art teaches that antisense molecules that exhibit less than 100% sequence identity to the target sequence produce unexpected results. Emery et al (2003, Current Biology 13:1768-1774) disclose experiments in which a target sequence of a micro-RNA was changed by two base-pairs. The altered base-pairs caused the complementary micro-RNA not to bind to the target sequence, which subsequently led to an increased expression of the target sequence's encoded protein (page 1769, right column, 2<sup>nd</sup> full paragraph).

In the absence of guidance, undue trial and error experimentation would be required for one of ordinary skill in the art to screen through the multitude of non-exemplified sequences, either by using non-disclosed fragments of a nucleic acid encoding the Arabidopsis Met1 protein as probes or by designing primers to undisclosed regions of a nucleic acid encoding the Arabidopsis Met1 protein and isolating or amplifying fragments, subcloning the fragments, producing expression vectors and transforming plants therewith, in order to identify those, if any, that when over-expressed in female germ line cells down-regulate one or more DNA methylating enzymes present in the plant.

Therefore, given the breadth of the claims; the lack of guidance and examples; the unpredictability in the art; and the state-of-the-art as discussed above, undue experimentation would be required to practice the claimed invention, and therefore the invention is not enabled.

Applicant's arguments filed 11/7/2005 have been fully considered but they are not persuasive.

Applicant contends that the Jacobsen et al reference would not lead one of ordinary skill in the art to conclude that claims drawn to downregulating DNA methylating enzymes would not be enabled (page 16 of Remarks, 3<sup>rd</sup> full paragraph). Applicant contends that the Jacobsen et

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al reference deals with down-regulating the Met1 gene in Arabidopsis and the subsequent hypermethylation of the Superman gene. Applicant contends that the instant claims are not drawn to the Superman gene (page 16 of Remarks, 2<sup>nd</sup> full paragraph). Applicant contends that U.S. patent 6,011,200 describes the use of a Met1 antisense sequence that was about 4300 nucleotides and that this sequence was successful in reducing the degree of DNA methylation (page 16 of Remarks, 3<sup>rd</sup> full paragraph). Applicant contends that Finnegan et al (1996, PNAS 93:8449-8454) used a 2550 nucleotide sequence from Met 1 in antisense orientation to successfully reduce DNA methylation (page 16 of Remarks, 3<sup>rd</sup> full paragraph). Applicant contends the office action mailed 10/25/2004 provides no explanation as to why data reported in Jacobsen would contradict the positive results of using antisense technology to reduce methylation (page 17 of Remarks, 1<sup>st</sup> paragraph). Applicant contends that one of ordinary skill could readily identify and isolate any and all non-exemplified Arabidopsis and Z. mays MET1 sequences (page 17 of Remarks, 3<sup>rd</sup> paragraph).

The Office contends that the Jacobsen et al reference was used to show that down-regulating DNA methylating enzymes does not always produce the expected results. This reference was not used to show non-enablement of antisense technology. The Jacobsen et al reference is a perfect reference illustrating the unpredictability of the claimed techniques. The reference discloses the down-regulation of a DNA methylating enzyme and the totally unexpected result that another sequence of DNA is hypermethylated. Given the fact that Applicant is claiming a multitude of non-exemplified sequences, one of ordinary skill in the art would have to screen through said multitude and produce constructs and expression vectors and transgenic plants and then screen through the thousands of plants to find those that have the

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claimed phenotype. This procedure becomes especially cumbersome given the unexpected results that are disclosed by Jacobsen et al.

The Office acknowledges the success of Finnegan et al using the 2550 nucleotide segment in antisense orientation, of the Arabidopsis Met1 gene to down regulate the corresponding endogenous gene in Arabidopsis. But, Applicant's claims are drawn to any partial sequence, which as discussed above, includes thousands of sequences because the office interprets "a partial sequence" to read on any two consecutive amino acids of the Met1 sequence. Again, undue trial and error experimentation would be required by one of skill in the art to practice the broadly claimed invention.

The Office contends that given the one disclosed sequence as discussed above, or even given the sequence of Finnegan et al, because Applicant's claims are drawn to any sequence encoding any two amino acids from Met 1, one of skill in the art would have to screen through thousands of sequences, and given the unpredictability as discussed above, undue trial and error experimentation would be required.

Applicant contends the Fourgoux-Nicol reference is not relevant to the claimed subject matter (page 18 or Remarks, 1<sup>st</sup> and 2<sup>nd</sup> full paragraphs).

The Office contends that this reference was used to show that protocols that use "standard" techniques, which in this case are hybridization reactions used to isolate nucleic acid sequences, do not always produce expected results. This reference was used to demonstrate unpredictability in the art.

Applicants contend that there is a high degree of sequence identity in the MET1 sequence (page 19 of Remarks, 2<sup>nd</sup> paragraph). Applicant contends there is a high degree of sequence

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identity between the Arabidopsis and Zea mays Met1 sequence. Applicant recites specific percent identities for different regions of the DNA molecule encoding the MET1 protein.

Applicant contends an alignment is attached (page 19 of Remarks, 2<sup>nd</sup> paragraph).

The Office contends that an alignment was not found in papers filed 11/7/2005. The Office contends that all Applicant has done is to recite specific percent identities between the Arabidopsis MET1 sequence and the homologous sequence in Zea mays pertaining to specified and non-specified regions. In regards to enablement of using sequences that are not 100% identical to the target sequence, Emery et al teach that as little as a one base pair difference between an antisense sequence and the target sequence can result in a non-operative antisense mechanism. (See office action mailed 10/25/2004).

Applicants contend co-suppression would have been well known to one of ordinary skill in the art (page 19 of Remarks, 3<sup>rd</sup> paragraph).

The Office contends that co-suppression is well known in the art and is predictable for sequences that are 100% identical to their target sequence. But, for sequences that are not 100%, the state-of-the-art teaches unpredictability of co-suppression. (See Gutterson et al).

In regards to the Emery et al reference, Applicant contends the MPEP restricts post filing-date references and can only be used “if individuals of skill in the art state that a particular invention is not possible years after the filing date” (page 20 of Remarks, 1<sup>st</sup> full paragraph). Applicant contends no such statement is found.

The Office contends that Applicant’s method is disclosed in the Emery et al reference because Applicant is relying on an antisense mechanism to produce the desired phenotype. According to the MPEP §2164.05(a) “In re Wright, 999 F.2d 1557, 1562, 27 USPQ2d 1510,



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1513-14 (Fed. Cir. 1993) an article published 5 years after the filing date of the application adequately supported the examiner's position that the physiological activity of certain viruses was sufficiently unpredictable so that a person skilled in the art would not have believed that the success with one virus and one animal could be extrapolated successfully to all viruses with all living organisms". In the instant application, Applicants are relying on antisense technology to produce the desired phenotype and Emery et al state a 100% sequence match is required between the introduced sequence and its target.

Applicant contends the citing of *In re Wright* in regards to the Mazzolini et al reference is inappropriate because *In re Wright* dealt with obviousness (page 20 of Remarks, 2<sup>nd</sup> full paragraph).

The Office contends this is a moot point because the Mazzolini et al reference was not used in the present office action.

### ***Double Patenting***

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 20-21, 62-67, 69, 71, 76-78, 80-93 are provisionally rejected under the judicially created doctrine of double patenting over claims 36-43, 45-55, 57-69 and 71-73 of copending Application No. 10/702,341. This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

The subject matter claimed in the instant application is fully disclosed in the referenced copending application and would be covered by any patent granted on that copending application since the referenced copending application and the instant application are claiming common subject matter, as follows: Claims 20-21, 62-67, 69, 71, 76-78, 80-93 of the instant application are drawn to a method for the production of modified endosperm, which comprises the step of introducing a nucleic acid molecule into a plant, the nucleic acid molecule comprising one or more regulatory sequences targeting expression in female germ line cells and a sequence whose transcription product comprises a partial or full-length Arabidopsis MET1 sequence, wherein the introduced nucleic acid is effective for down-regulating one or more DNA methylating enzymes present in the plant, whereby the degree of DNA methylation of nucleic acid in the plant is reduced as compared to a control, or wherein the transcription product comprises an antisense nucleic acid, or wherein the introduced nucleic acid is a partial or full-length Z. mays sequence orthologous to the Arabidopsis MET1, or wherein the nucleic acid is a full or partial sense copy of a DNA methylating enzyme already present in the plant, or wherein the plant is a dicotyledonous plant.

Claims 36-43, 45-55, 57-69 and 71-73 of copending Application No. 10/702,341 are drawn to a method for the production of seeds, comprising the step of permitting self-pollination or cross-pollination of a plant comprising a nucleic acid sequence effective for reducing levels of

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general DNA methylation, operably linked to a promoter, wherein seeds that develop on said plant have increased mean seed weight compared to the mean seed weight of seeds from a control plant, or wherein said nucleic acid sequence comprises a sense or antisense sequence having at least 80% identity to DNA that encodes the Arabidopsis DNA methyltransferase 1 (MET1) enzyme, or wherein said sequence is a homologue of Arabidopsis DNA methyltransferase 1 enzyme, or wherein said promoter is a gynoeceium-specific promoter or a female germ line promoter, or wherein said seeds have a mean seed weight that is at least 47% or 81% greater than the mean seed weight from control plants; a transgenic plant comprising said sequence or wherein said plant produces seed that have a mean seed weight that is at least 47% or 81% greater than the mean seed weight from control plants.

Because seeds are produced as a result of pollination, and because endosperm development is a normal process involved in seed development, it would be inherent that the methods of the instant application include a pollination step. Therefore, because the starting materials and method steps of the two applications are the same, the claims of the instant application are drawn to the same invention as claimed in the '341 application.

Furthermore, there is no apparent reason why applicant would be prevented from presenting claims corresponding to those of the instant application in the other copending application. See *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968). See also MPEP § 804.

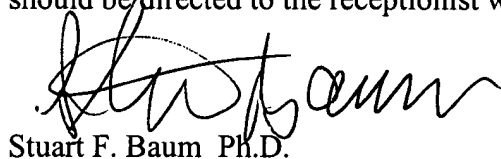
9. No claims are allowed.

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10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stuart F. Baum whose telephone number is 571-272-0792. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached at 571-272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

A handwritten signature in black ink, appearing to read 'Stuart F. Baum', is written over the printed name.

Stuart F. Baum Ph.D.

Patent Examiner

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January 20, 2006